AMENDMENTS TO THE SPECIFICATION:

Page 6, please amend the paragraph beginning at line 26 and ending at line 36 as follows:

(A) Schematic representation of IRF-3 point mutations. Thick solid lines and thin dashed lines indicate included and excluded sequences, respectively. The N-terminal IRF homology domain, the Nes element and C-terminal IRF association domain are indicated. Amino acids residues from 382 to 414 and from ~~141~~ 139 to ~~147~~ 145 are shown (SEQ ID NO:1). The amino acids targeted for alanine or aspartic acid substitution are shown in large print. The point mutations are indicated below the sequence: (2A: S396A/S398A; 3A: S402A/T404A/S405A; 5A: S396A/S398A/S402A/T404A/S405A); 5D S396D/S398D/S402D/T404D/S405D; J2A: S385A/S386A; NES: ~~S145A/S146A~~ S143A/S144A).

(B) Expression plasmids (5μg each) encoding wild type and

Page 9, please amend the paragraphs beginning at line 17 and ending at line 28 as follows:

Figure 10. The cDNA sequence encoding IRF-3(5D), together with the amino acid sequence of IRF-3(5D) (SEQ ID NO:1).

Figure 11. Transactivation study as described in Figure 6, using the IFNβ-CAT reporter plasmid to indicate the activity of various forms of IRF-3 and IRF-7 and binary mixtures thereof.

Figure 12. The cDNA sequence encoding IRF-7A(2D), together with the amino acid sequence of IRF-7A(2D) (SEQ ID NO:8).

Figure 13. The cDNA sequence encoding the IRF-7(1-246)/IRF-3(5D) (132-427) chimeric protein, together with the amino acid sequence of the IRF-7(1-246)/IRF-3(5D) (132-427) chimeric protein (SEQ ID NO:10).

Page 11, please amend the partial paragraph beginning at line 1 and ending at line 16 as follows:

having aspartic acid residues in at least one of positions 396, 398, 402, 404 and 405 of the sequence, more preferably in positions 396, 398, 402, 404 and 405 of the sequence (IRF-3(5D)) ~~(Figure 10)~~ (SEQ ID NO:1). The preferred mutant form of IRF-7 is that having aspartic acid residues in at least one of positions 477 and 479 of the sequence, more preferable in positions 477 and 479 of the sequence (IRF-7(2D)) ~~(Figure 12)~~ (SEQ ID NO:8).

Also within the scope of the invention are chimeric proteins comprising a carboxy-terminus domain of one modified IRF protein, modified as discussed above, and an amino-terminal domain of another IRF protein. Preferably, the amino-terminus of IRF-7 is fused to the carboxy-terminus of modified IRF-3. It is more preferred that the carboxy-terminus of modified IRF-3 is that of IRF-3(5D). Even more preferred is a chimeric protein comprising residues 1 to 246 of IRF-7 and residues 132 to 427 of IRF-3(5D) ~~(Figure 13)~~ (SEQ ID NO:10).

Page 11, please amend the partial paragraph beginning at line 22 and ending at line 31 as follows:

Nucleotide sequences within the scope of the invention are those which encode a protein of the invention. Preferably, the nucleotide sequence is a coding DNA sequence as defined in ~~Figure 10~~ SEQ ID NO:1 or a DNA sequence which is hybridizable under stringent conditions with the complement of the coding DNA sequence of ~~Figure 10~~ SEQ ID NO:1, which DNA encodes IRF-3(5D). Also, preferably, the nucleotide

sequence is a coding DNA sequence as defined in ~~Figure 12~~ SEQ ID NO:8 or a DNA sequence which is hybridizable under stringent conditions with the complement of the coding DNA sequence in ~~Figure 12~~ SEQ ID NO:8, which DNA encodes IRF-7(2D). Also

Page 11a, please amend the partial paragraph beginning at line 1 and ending at line 5 and the paragraph beginning at line 7 and ending at line 9 as follows:

preferably, the nucleotide sequence is a coding DNA sequence as defined in ~~Figure 13~~ SEQ ID NO:10 or a DNA sequence which is hybridizable under stringent conditions with the complement of the coding DNA sequence of ~~Figure 13~~ SEQ ID NO:10, which DNA encodes IRF-7(1-246)/IRF-3 (132-427) chimeric protein.

A combination of IRF-3 deletion and point mutations localized the inducible phosphorylation sites to the region -ISNSHPLSLTSDQ- (SEQ ID NO:3) between amino acids 395 and 407; point mutation

Page 16, please amend the paragraph beginning at line 29 and ending at line 37 as follows:

Similarities and differences exist between the observed degradation of IRF-3 and the mechanism of $I_\kappa B_\alpha$ degradation. The C-terminal phosphorylation of IRF-3 as a consequence of virus infection is required for its subsequent degradation based on the deletion and point mutation analysis of the region -ISNSHPLSLTSDQ- (SEQ ID NO:3) between amino acids 395 and 407. Minimally, phosphorylation of Ser-396 and Ser-398 are required for subsequent degradation, although Ser-402, Ser-404 and Ser-405 may represent secondary phosphorylation sites.

Page 22, please amend the partial paragraph beginning at line 1 and ending at line 19 as follows:

(PMSF)] and were resuspended in Buffer A containing 0.1% NP-40. Cells were then chilled on ice for 10 minutes before centrifugation at 10,000 g. Pellets were then resuspended in Buffer B (20 mM HEPES, pH 7.9; 25% glycerol; 0.42 M NaC1; 1.5 mM $MgC1_2$; 0.2 mM EDTA; 0.5 mM DTT; 0.5 mM PMSF; 5 μg/ml leupeptin; 5 μg/ml pepstatin; 0.5 mM spermidine; 0.15 mM spermine; and 5 μg/ml aprotinin). Samples were incubated on ice for 15 minutes before being centrifuged at 10,000 g. Nuclear extract supernatants were diluted with Buffer C (20 mM HEPES, pH 7.9; 20% glycerol; 0.2 mM EDTA; 50 mM KC1; 0.5 mM DTT; and 0.5 mM PMSF). Nuclear extracts were subjected to EMSA by using a 32P-labelled probe corresponding to the PRDIII region of the IFN-β promoter (5' -GGAAAACTGAAAGGG-3') (SEQ ID NO:6) or the ISRE region of the ISG-15 promoter (5'-GATCGGGAAAGGGAAACCGAAACTGAAGCC-3') (SEQ ID NO:7). The resulting protein-DNA complexes were resolved by 5% polyacrylamide gel and exposed to X-ray film. To demonstrate the specificity of protein-DNA complex formation, 125-fold molar excess of unlabelled oligonucleotide was added to the nuclear extract before adding labelled probe.

C7

Page 24, please amend the partial paragraph beginning at line 32 and ending at line 37 as follows:

C8

Thus, by deletion analysis, a phosphorylation domain of IRF-3 protein was localized to the region -ISNSHPLSLTSDQ- (SEQ ID NO:3) between amino acids 395 and 407. Point mutations in the several putative Ser and Thr phosphorylation residues within this region were generated in the full length protein and the Δ9-133 (ΔN) protein (Fig. 4A). In the IRF-3 cDNA encoding